## REMARKS

Reconsideration of this application is respectfully requested.

Claims 2-24 and 245-260 were previously pending in this application. Claims 2-24 have been canceled. Claims 249, 251, 253, 257, 259 and 260 have been amended above. No claims have been added. Accordingly, claims 245-260 as amended are presented for further examination.

The first page (line 1) of the specification has been amended by inserting information cross-referencing this divisional application with the prior parent application, Serial No. 08/574,443, filed on December 15, 1995. The parent application was revived for purposes of continuity so that the present divisional application could be filed.

Several informalities in the specification have been corrected. These include changes on pages 9, 64, 81, 105, 109, 114, 123, 127, 134, 151, 159, 180 and 181, none of which is believed to have inserted new matter into Applicants' disclosure. Referring to the aforementioned page 81 (line 7), Applicants have corrected the description of an incompatible cell to mean "a cell *incapable* of processing RNA by removal of the processing element." The definition of an incompatible cell is in contrast to the definition of a compatible cell that precedes it. In the preceding lines on page 81, a compatible cell is defined as "a cell capable of processing RNA by removal of the processing element." See page 81, lines 5-6. In clarifying the definition of an incompatible cell, Applicants have corrected an obvious error in the specification that is clear from its context. Thus, no new matter has been inserted thereby.

Minor changes have also been made to five claims, including claims 249, 251, 253, 257 and 259. These minor changes affect only the Markush language in the foregoing claims. It is believed that the amended claim language in these claims conforms to the accepted proper usage under U.S. patent practice. In claim 260, the word "composition" has been changed to -- construct -- .

Entry of the above amendments to the specification and claims is respectfully requested.

**Objection to Patent Drawings**

Acknowledgement is made of the Notice of Draftperson's Patent Drawings Review that was issued in connection with this application. Formal drawings will be submitted as soon as allowable subject matter has been indicated in this application.

**Submission of Sequence Listing**

Applicants are filing concurrently with this Amendment a response to the Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

**The Rejection for Double Patenting Under 35 U.S.C. §101**

Claims 2-24 stand provisionally rejected under 35 U.S.C. §101 as claiming the same invention as that of claims 2-24 of copending Application Nos.: 08/978,632, 08/978,633, 08/978,634, 08/978,635, 08/978,637, 08/978,638, 08/978,639, and 08/574,443. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

As indicated above, claims 2-24 have now been canceled as they should have been when claims 245-313 were presented in Applicants' November 25, 1997 Preliminary Amendment. Any inconvenience caused by this oversight is sincerely regretted.

In view of the cancelation of claims 2-24, Applicants respectfully request withdrawal of the double patenting rejection.

**The Rejection for Obviousness-Type Double Patenting**

Claims 255, 257, 259 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 245-247 of copending Application No. 08/978,635. In the Office Action (page 3), the Examiner stated:

> Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to the nucleic acid construct "which when introduced into a cell produces a nucleic acid product . . ." and claims 245-247 of '635 are drawn to "a process for . . . expressing a nucleic acid product in a cell . . ." The claimed construct is obvious from the method claimed.
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> This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

In response, Applicants and the present Assignee point out that it is their intention to maintain a line of demarcation between the subject matter of this application and that of their copending Serial No. 08/978,635. Because both applications are being presently prosecuted and it is uncertain at this point in time what will be the subject matter and language in any claims to be issued therefrom, Applicants respectfully request that the rejection for obviousness-type double patenting be held in abeyance until such time as subject matter is deemed allowable in either or both applications.

**The Rejection Under 35 U.S.C. §112, Second Paragraph**

Claims 2-21 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the Office Action (page 4), the Examiner stated:

> Claims 2-21 are indefinite because they depend from canceled claim 1. Therefore, claims 2-21 do not depend on any independent claim.

The Examiner's comments above have been well taken with respect to claims 2-21, leading to the cancelation of the former claims, including claims 22-24 (see the opening remarks of this Amendment).

In light of the cancelation of claims 2-24, it is respectfully requested that the rejection under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

**The Rejection Under 35 U.S.C. §112, First Paragraph**

Claims 2-21 and 245-260 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In the Office Action (pages 4-7), the Examiner stated:

> The constructs taught in the claims 2-24 are broadly drawn to a multitude of possible nucleic acid based constructs for use in a cell to produce a product (and in any context, *in vivo* or *in vitro),* comprising: (1) the construct as linear or circular, (2) the construct as comprising 1,2 or 3 strands, (3) comprising a terminus, a polynucleotide tail which can hybridize, (4) composed of RNA or DNA or combinations, (5)containing chemically modified nucleotides or analogs, (6) containing non-nucleic acid entities composed of polymers or ligands or a combination, (7) further specifying the natural and synthetic polymers, the synthetic homo- or heteropolymer with a net charge, (8) the construct imparting a "further biological activity" by the modified nucleotide, analog, entity, ligand or combination of those, further defined as nuclease resistance, cell recognition, cell binding, and cellular or nuclear localization or a combination, (9) a ligand attached to one of the modified nucleotides, etc. of claim 1, further described as attached to a "segment" or "tail" of the construct, and further defined as being a macromolecule or small molecule or combination. Claims 22-24 describe a second construct "which when present in a cell produces a product, said construct being bound non-ionically to an entity comprising a chemical modification or a ligand."
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> Claims 245-254 are drawn to another broad genus of nucleic acid constructs for co-expression of a non-native polymerase and another nucleic acid sequence from the construct in a cell, again in any context, *in vivo* or *in vitro*. Dependent claims include the limitations: (1) a recognition site for the polymerase, (2) where the recognition site

is complementary to a primer for the polymerase, (3) where the primer is tRNA, (4) where the polymerase is DNA polymerase, RNA polymerase, reverse transcriptase, or a combination, (5) where the RNA polymerase is a bacteriophage RNA polymerase, either T3, T7, SP6 or a combination, (6) a promoter for the RNA polymerase, (7) the nucleic acid produced is DNA, RNA, or a hybrid, chimera, or a combination and is sense or antisense DNA or RNA.

Claims 255-260 are drawn to another broadly claimed nucleic acid based construct for producing a non-native processing element product in a cell which is substantially removed during processing (again, the claims could be read in any context, *in vivo* or *in vitro*). The limitations further include: (1)an RNA processing element, selected from an intron, a polyadenylation and a capping element, or a combination, (2) a single stranded nucleic acid product, (3) a nucleic acid product selected from antisense RNA, antisense DNA, sense RNA, sense DNA, a ribozyme and a protein binding nucleic acid sequence or a combination, (4) and wherein said protein binding nucleic acid sequence comprises a decoy that binds a protein required for viral assembly or replication.

The specification teaches several constructs designed for entry into a cell and expression of one or more sequences to perform a biological function such as antisense inhibition of a nucleic acid. Specifically, several CHENAC constructs are taught prophetically, and pictured in figures 1-13 as vector based constructs constructed by using modified nucleic acid regions and designed to provide improved entry into a cell by way of improved construct-cell interaction. A second group of nucleic acid fused with antibody based constructs are taught prophetically and shown in figures 14-21. Preparation of multimeric insulin by means of nucleic acid hybridization is further taught prophetically and shown in figures 22-23. No exemplification for such constructs is taught in the specification as filed.

Furthermore, vectors ultimately designed for antisense inhibition of HIV in cells by co-expression of antisense DNA under control of a T7 promoter with a T7 polymerase (represented in figures 24-49) are taught and supported by *in vitro* data. Specifically, construction of the M13 phage vectors pRT-A, pRT-B, and pRT-c are taught which contain the coding sequence for the T7 RNA polymerase driven by the RSV promoter and with an SV40 intron sequence that will be spliced out to form a functional polymerase enzyme and each respective construct also having the antisense A, B, and C sequences driven by a T7 promoter and terminated by a T7 terminator. A modified version of the pINT-3 construct (the parent vector of pRT-A, B and C vectors before insertion of the antisense sequences) is taught where a polylinker is inserted behind the poly-A tail of the T7 polymerase gene for subsequent sub-cloning of the lacZ gene in this instance to form pINT-LacZ. The result upon introduction in a eukaryotic cell would be synthesis of the T7 polymerase from the RSV promoter which in turn acts upon the T7 promoter to synthesize B-galactosidase.

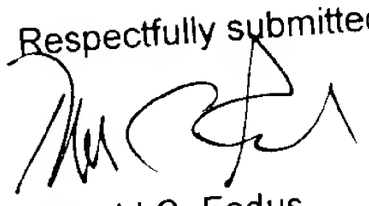
Continuing on pages 7-9, the Examiner stated:

4. a Declaration Under 37 C.F.R. §1.821(g) attesting that the content of the paper copy and computer readable copy are the same and include no new matter.

No fee is believed due in connection with this Communication or the documents or items submitted herewith other than the fee payment authorized in the Request For an Extension Of Time (Three Months Under 37 C.F.R. .§1.136(a). If any other fee or fees are due, however, the Patent and Trademark Office is hereby authorized to charge the amount of any such fee to Deposit Account 05-1135, or to credit any overpayment thereto.

If helpful to processing this Communication, the undersigned may be contacted by telephone at (212) 583-0100 during the daytime hours.

Respectfully submitted,



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